UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/664,603	09/17/2003	Guy A. Roulcau	GOUD:023USD1	3929

7590 11/28/2006

Michael R. Krawzsenek
Fulbright & Jaworski L.L.P.
600 Congress Avenue, Suite 2400
Austin, TX 78701

EXAMINER	
LIU, SUE XU	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 11/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/664,603	ROULEAU'ET AL.	
	Examiner	Art Unit	
	Sue Liu	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-33* is/are pending in the application.

4a) Of the above claim(s) *21,23,26 and 29-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-20,22,24,25,27 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/3;5/16;10/4*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Claims 1-13 have been cancelled as filed on 9/17/03;

Claims 14-33 are currently pending;

Claims 21, 23, 26 and 29-33 have been withdrawn;

Claims 14-20, 22, 24, 25, 27 and 28 are being examined in this application.

Election/Restrictions

1. Applicant's election with traverse of Group I (Claims 14-28) in the reply filed on 9/25/06 is acknowledged. The traversal is on the ground(s) that there is no serious burden to search all the inventions in the application. Applicants also argue that the different nucleic acids share similar structure, and thus restriction between the different nucleic acid sequences is improper. This is not found persuasive because the distinct inventions would require different searches in each of the respective classes and/or subclasses. The searches required for each group are not co-extensive thus requiring a burdensome search. Additionally, different patentability considerations are involved for each group. For example, a patentability determination for Group 1 would involve a determination of the patentability of a method for assaying sodium channels encoded by various nucleic acids using test agents, while a patentability determination for Group 2 would involve a determination of the patentability of a therapeutic method for diseases such as epilepsy or other neurological disorders. These considerations are very different in nature. The different steps of the Group 2 method would require separate searches, and would not be co-extensive for Group 1 method.

Applicants also traversed the restriction between the different nucleic acid sequences by stating that the different sequences "share several functional and structural features". (Reply, 9/25/06; p. 8, para 1). However, applicants have not provided any evidence to show that all of the nucleic acids sequences recited in the instant claims (SEQ ID Nos: 65, 66, 69-98, and 400-407) share the same structure or even the same core structure. A brief survey of all the different nucleic acids indicates that they have different lengths ranging from 13 nucleotides to 9112 nucleotides. The different SEQ ID Nos also have different nucleic acid sequences that are not substantially homologous, and do not share the same core structure. For example, SEQ ID Nos 72 and 73 do not share significant sequence similarity as indicated by BLAST alignment (see the attached BLAST Result; downloaded 11/13/06). Furthermore, the instant specification discloses that the various genes (nucleic acids) and/or proteins recited in SEQ ID Nos: 1-98 are "structurally distinct sodium channel alpha subunit isoforms in brain" (emphasis added). (pp. 5-6, bridging para). Thus, the different nucleic acid sequences represented by the different SEQ ID Nos are structurally distinct. Searches of different sequences would create an undue search burden on the Office, because separate sequence searches have to be run in different sequence databases for each individual sequence.

Applicants also cited the passage of MPEP 2434 that indicates "up to 10 independent and distinct nucleotide sequences will be examined in a single application without restriction." (Reply, p. 7). Contrary to applicant's interpretation, the phrase "up to 10" does not provide a minimum number of distinct sequences, rather it provides a maximum limit of 10 distinct sequences to be searched if no serious burden is required. However, in this case, a serious search burden has been established as discussed above.

Thus, the restriction requirement is still deemed proper and is therefore made FINAL.

2. Claims 21, 23, and 29-33 as well as SEQ ID Nos 66 and 69-98 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 9/25/06.

3. Applicant's election with traverse of the following species:

A. Idiopathic Generalized Epilepsy (IGE);

B. Chemical Compound (or agent) (see specification at page 20, lines 22-24);

C. Inactivation;

D. Human SCN3A; and

E. Cell-Free System

in the reply filed on 9/25/2004 is acknowledged. The traversal is on the ground(s) that the species (especially requirement B.) "should not be considered essential elements to assess whether the claimed assays ... are patentable" (Reply, p. 9). This is not found persuasive because the instant claims recite the step of using a compound. That is the compound offers a structural limitation to the claimed method step. The different species of compounds (such as different chemical compounds) would be structurally different from each other. Therefore the different species represent patentably distinct subject matter.

Accordingly, Claim 26 is withdrawn due to non-elected species.

Priority

4. This application is a DIVISIONAL of U.S. Patent Application Nos. 09/718,355 (filed 11/24/2000), which claims priority benefit to a US provisional application 60/167,623 (filed 11/26/1999).

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description Rejection

6. Claims 14-20, 22, 24, 25, 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims recite an assay for selecting a compound useful for treating epilepsy or other neurological disorders which modulates inactivation of a sodium channel comprising:

a) an SCN3A nucleic acid sequence which encodes an SCN3A sodium channel or a functional fragment thereof; and

b) assaying a function of said sodium channel; wherein a compound is selected when a difference is observed between the inactivation of said sodium channel in the presence of a test agent, as compared to in the absence thereof.

To satisfy the written description requirement, applicants may convey reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.

Applicants may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. See, e.g., Vas-Cath, 935 F.2d at 1565, 19 USPQ2d at 1118.

The written description requirement of 35 U.SC. 112 exists independently of enablement requirement, and the requirement applies whether or not the case involves questions of priority. The requirement applies to all inventions, including chemical inventions, and because the fact that the patent is directed to method entailing use of compound, rather than to compound per se, does not remove patentee's obligation to provide a description of the compound sufficient to distinguish infringing methods from non-infringing methods. See Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 920-23, 69 USPQ 2d 1886, 1890-93 (Fed. Cir. 2004).

With regard to the description requirement, applicants' attention is invited to consider the decision of the Court of Appeals for the Federal Circuit, which holds that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it form other materials." University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1405 (1997), quoting Fiers v. Revel, 25 USPQ2d 1601, 1606

(Fed. Cir. 1993) (bracketed material in original) [The claims at issue in University of California v. Eli Lilly defined the invention by function of the claimed DNA (encoding insulin)].

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species or by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical an/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F. 3d at 1568, 43 USPQ2d at 1406.

The instant claims (especially Claims 14 and 16) are drawn to a method comprising method steps of using a genus of compounds and a genus of SCN3 sodium channels nucleic acids. Neither the instant specification nor the claims have demonstrated common structure and/or function for the claimed genuses of compounds and SCN3A sodium channels nucleic acids. In addition, no representative numbers of species for each claimed genus is provided to show possession of the claimed genus of genes and genus of precursor molecules.

The instant specification is only prophetic in term of the "compound" that is used for the assay method. The instant disclosure states that the "terms "molecule", "compound", "agent" or "ligand" are used interchangeably and broadly to refer to natural, synthetic or semi-synthetic molecules or compounds" (p. 20, lines 20+). That is the term "compound" or "agent" as recited in the instant claims encompasses almost any compound including various organic and inorganic chemical compounds as well as biological macromolecules such as nucleic acid and proteins.

These different molecules do not share common structure, function, and/or properties. The instant specification also does not provide representative number of species of the "compound" that can be assayed with the claimed "sodium channel".

The claimed "SCN3A" sodium channel nucleic acids are not limited to a single nucleic acid (such as SEQ ID No 65). The claim recitation encompasses any "SCN3A" from any species (such as different mammalian species as recited in Claim 15), and any allelic variant thereof as recited in Claim 22. The instant specification discloses that the "SCN3A" can be represented by SEQ ID Nos: 1-98" (pp. 5-6, bridging para). However, these examples of the SCN3A sodium channel nucleic acid sequences have different nucleic acid sequences that are not substantially homologous, and do not share the same core structure. For example, SEQ ID Nos 72 and 73 do not share significant sequence similarity as indicated by BLAST alignment (see the attached BLAST Result; downloaded 11/13/06). The instant disclosure does not provide a common core structure and/or representative number of species to show possession of the entire genus of SCN3A sodium channel nucleic acids or proteins. The instant specification only provides a few examples of SCN3A mutants (Example 5 of the instant spec.), but no examples of assaying the mutants or wild-type SCN3A sodium channels with various compounds.

Although certain compounds such as the ones listed in a review by Kohling (Epilepsia. Vol. 43 (11): 1278-1295; 2002) have been used in various assays with sodium channels, the art does not teach that any compounds can be screened with sodium channel, or that any sodium channel (such as various mutants of SCN3A) can be used in a screening assay. For examples, Kohling teaches that there are different types of assays (such as patch clamp) (p. 1281; p. 1285, right col.), and these assays may or may not produce conclusive results (e.g. "Analysis of spike

shape, repetitive firing properties, toxin binding, or sodium uptake only indirectly reflects sodium channel involvements"; p. 1285, right col.). Further, Kohling teaches some drugs have effects on sodium current but at concentrations beyond therapeutic levels, and "thus the mechanism of action cannot be considered to consist of sodium current modulation" (p. 1285, right col.). That is the effects of different drugs (or compounds) on the sodium channel may or may not be conclusive observed by the various type of sodium channel assays. To further illustrate this, the reference reviews various drugs that have been studied (p. 1286+), and from which ESM (p. 1287, right col.) was shown to have different effects on the activity of the sodium channel depending on the how the drug is applied. Valproate was also shown to have "notable" effects on sodium current (produced by sodium channel) only in assays where the drug is internally applied (p. 1289, right col., para 4).

The predictability of suitable assays for monitoring ion channel activity is also discussed in Birch et al (Drug Discovery Today. Vol. 9 (9): 410-418; 2004). For examples, the reference teaches the problems associated with various assay methodologies (p. 414, Table 3; p. 415, Table 4). As indicated by the Tables of the reference, there are various factors that can influence the success of a sodium channel assay (such as requirement for high channel expression; Table 3). These effects of these factors are highly unpredictable for different assays as indicated by the reference, and thus rendering the sodium channel assays unpredictable.

Therefore, applicants are not in possession of the genus of compounds and the genus of SCN3A sodium channel (nucleic acids and/or proteins) of the claimed method. Applicant's claimed scope represents only an invitation to experiment regarding possible compounds and sodium channels that can be used with the claimed method.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

The instant claims also recite a method of assaying sodium channel using a cell free system (Claim 27). However, the instant specification does not provide adequate written description to indicate possession of such a method. The instant disclosure only prophetically states that the assay can be accomplished using cell free systems, and provided one example of a binding assay (p. 42, lines 6+ of the spec.), which do not provide guidance on the detection of the activity of the tested sodium channel. The art also does not provide much guidance in measuring sodium channel activity using cell free systems. Almost all of the sodium channel assays are conducted using intact cell systems, as demonstrated by Kohling and Birch et al. Birch et al also teach that detection of sodium channel activity such as electrical current changes, and ion concentration changes require an intact membrane that can allow the generation of membrane potentials (p. 413, left col. of Birch). In other words, without at least an intact membrane to compartmentalize, differences in voltage or ion concentration cannot be accomplished.

Thus, the instant specification and the claims have not demonstrated the possession of a method that use cell free system to monitor the activity of a sodium channel effected by a compound.

Scope of Enablement Rejection

7. Claims 14-20, 22, 24, 25, 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for assaying certain SCN3A sodium channels using certain compounds/agents, does not reasonably provide enablement for using any other SCN3A sodium channels and/or variants thereof with any other compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. §112, first paragraph, have been described *In re Wands*, 8 USPQ2d 1400(1988). They are:

1. The breadth of the claims;
2. The nature of the invention;
3. The state of the prior art;
4. The predictability or lack thereof in the art
5. The level of skill in the art;
6. The amount of direction or guidance present;
7. The presence or absence of working examples;
8. The quantity of experimentation needed.

The breadth of the claims/The nature of the invention

The instant claims (especially Claims 14 and 16) are drawn to a method comprising method steps of using a genus of compounds and a genus of SCN3 sodium channels nucleic acids. Neither the instant specification nor the claims have demonstrated common structure and/or function for the claimed genuses of compounds and SCN3A sodium channels nucleic

acids. In addition, no representative numbers of species for each claimed genus is provided to show possession of the claimed genus of genes and genus of precursor molecules.

The instant specification is only prophetic in term of the "compound" that is used for the assay method. The instant disclosure states that the "terms "molecule", "compound", "agent" or "ligand" are used interchangeably and broadly to refer to natural, synthetic or semi-synthetic molecules or compounds" (p. 20, lines 20+). That is the term "compound" or "agent" as recited in the instant claims encompasses almost any compound including various organic and inorganic chemical compounds as well as biological macromolecules such as nucleic acid and proteins. These different molecules do not share common structure, function, and/or properties. The instant specification also does not provide representative number of species of the "compound" that can be assayed with the claimed "sodium channel".

The claimed "SCN3A" sodium channel nucleic acids are not limited to a single nucleic acid (such as SEQ ID No 65). The claim recitation encompasses any "SCN3A" from any species (such as different mammalian species as recited in Claim 15), and any allelic variant thereof as recited in Claim 22. The instant specification discloses that the "SCN3A" can be represented by SEQ ID Nos: 1-98" (pp. 5-6, bridging para). However, these examples of the SCN3A sodium channel nucleic acid sequences have different nucleic acid sequences that are not substantially homologous, and do not share the same core structure. For example, SEQ ID Nos 72 and 73 do not share significant sequence similarity as indicated by BLAST alignment (see the attached BLAST Result; downloaded 11/13/06). The instant disclosure does not provide a common core structure and/or representative number of species to show possession of the entire genus of SCN3A sodium channel nucleic acids or proteins. The instant specification only provides a few

examples of SCN3A mutants (Example 5 of the instant spec.), but no examples of assaying the mutants or wild-type SCN3A sodium channels with various compounds.

The instant claims also recite a method of assaying sodium channel using a cell free system (Claim 27). However, the instant specification only prophetically states that the assay can be accomplished using cell free systems, and provides one example of a binding assay (p. 42, lines 6+ of the spec.), which does not provide any guidance on how to detect the activity of the tested sodium channel.

The state of the prior art/ The predictability or lack thereof in the art

The art does teach certain compounds such as the ones listed in a review by Kohling (Epilepsia. Vol. 43 (11): 1278-1295; 2002) have been used in various assays with sodium channels, however, the art does not teach that any compounds can be screened with sodium channel, or that any sodium channel (such as various mutants of SCN3A) can be used in a screening assay. For examples, Kohling teaches that there are different types of assays (such as patch clamp) (p. 1281; p. 1285, right col.), and these assays may or may not produce conclusive results (e.g. "Analysis of spike shape, repetitive firing properties, toxin binding, or sodium uptake only indirectly reflects sodium channel involvements"; p. 1285, right col.). Further, Kohling teaches some drugs have effects on sodium current but at concentrations beyond therapeutic levels, and "thus the mechanism of action cannot be considered to consist of sodium current modulation" (p. 1285, right col.). That is the effects of different drugs (or compounds) on the sodium channel may or may not be conclusive observed by the various type of sodium channel assays. To further illustrate this, the reference reviews various drugs that have been

studied (p. 1286+), and from which ESM (p. 1287, right col.) was shown to have different effects on the activity of the sodium channel depending on the how the drug is applied. Valproate was also shown to have "notable" effects on sodium current (produced by sodium channel) only in assays where the drug is internally applied (p. 1289, right col., para 4).

The predictability of suitable assays for monitoring ion channel activity is also discussed in Birch et al (Drug Discovery Today. Vol. 9 (9): 410-418; 2004). For examples, the reference teaches the problems associated with various assay methodologies (p. 414, Table 3; p. 415, Table 4). As indicated by the Tables of the reference, there are various factors that can influence the success of a sodium channel assay (such as requirement for high channel expression; Table 3). These effects of these factors are highly unpredictable for different assays as indicated by the reference, and thus rendering the sodium channel assays unpredictable.

Therefore, applicants are not in possession of the genus of compounds and the genus of SCN3A sodium channel (nucleic acids and/or proteins) of the claimed method. Applicant's claimed scope represents only an invitation to experiment regarding possible compounds and sodium channels that can be used with the claimed method.

In term of using cell free system to monitor sodium channel activity, the art also does not provide much guidance in measuring sodium channel activity using cell free systems. Almost all of the sodium channel assays are conducted using intact cell systems, as demonstrated by Kohling and Birch et al. Birch et al also teaches that detection of sodium channel activity such as electrical current changes, and ion concentration changes require an intact membrane that can allow the generation of membrane potentials (p. 413, left col. of Birch). In other words, without

at least an intact membrane to compartmentalize, differences in voltage or ion concentration cannot be accomplished.

The above discussion only illustrated a few problems with selecting compounds by assaying sodium channels activities. Although there may be suggested methods of overcoming these problems through non-routine experimentations, there are no predictable methods or solutions that would solve all the problems for any SCN3A sodium channel variants/mutants, and for assaying any compounds.

The level of one of ordinary skill

The level of skill would be high, most likely at the Ph.D. level.

The amount of direction or guidance present/The presence or absence of working examples

The instant specification is only prophetic in term of the "compound" that is used for the assay method. The instant disclosure states that the "terms "molecule", "compound", "agent" or "ligand" are used interchangeably and broadly to refer to natural, synthetic or semi-synthetic molecules or compounds" (p. 20, lines 20+). That is the term "compound" or "agent" as recited in the instant claims encompasses almost any compound including various organic and inorganic chemical compounds as well as biological macromolecules such as nucleic acid and proteins. These different molecules do not share common structure, function, and/or properties. The instant specification also does not provide representative number of species of the "compound" that can be assayed with the claimed "sodium channel".

The claimed "SCN3A" sodium channel nucleic acids are not limited to a single nucleic acid (such as SEQ ID No 65). The claim recitation encompasses any "SCN3A" from any species (such as different mammalian species as recited in Claim 15), and any allelic variant thereof as recited in Claim 22. The instant specification discloses that the "SCN3A" can be represented by SEQ ID Nos: 1-98" (pp. 5-6, bridging para). However, these examples of the SCN3A sodium channel nucleic acid sequences have different nucleic acid sequences that are not substantially homologous, and do not share the same core structure. For example, SEQ ID Nos 72 and 73 do not share significant sequence similarity as indicated by BLAST alignment (see the attached BLAST Result; downloaded 11/13/06). The instant disclosure does not provide a common core structure and/or representative number of species to show possession of the entire genus of SCN3A sodium channel nucleic acids or proteins. The instant specification only provides a few examples of SCN3A mutants (Example 5 of the instant spec.), but no examples of assaying the mutants or wild-type SCN3A sodium channels with various compounds.

In addition, the instant disclosure only prophetically states that the assay can be accomplished using cell free systems, and provided one example of a binding assay (p. 42, lines 6+ of the spec.), which do not provide guidance on the detection of the activity of the tested sodium channel.

The quantity of experimentation needed

Due to the unpredictabilities of assaying various SCN3A sodium channels with various compounds (using various assay methodologies), undue experimentation would be required. The art has not demonstrated all the possible SCN3A sodium channel variants that can be used in the

different assay systems with various compounds. The art has not demonstrated that any compound can be used to assay different activities of various sodium channels. In addition, the art has also not demonstrated the feasibility of using cell free systems in successfully monitoring sodium channel activities with various compounds. Thus, undue experimentation would be required for a person of ordinary skill in the art to use the claimed assay in its full scope.

Conclusion

Therefore based on the evidences as a whole regarding each of the above factors (e.g. factors 1-8), the specification, at the time the application was filed, does not satisfy the enablement requirement for the instant claimed method.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 14-20, 22, 24, 25, 27 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 recites the limitations "the presence of a test agent" (emphasis added) in line 8. There is insufficient antecedent basis for this limitation in the claim. It is not clear if the "test agent" is referring to the recited "compound" in the preceding lines or it is a different entity from the said compound. The method steps of Claim 14 also do not recite "a test agent" as well as "a compound".

Claim 16 recites the limitation "said test agent" in line 8. There is insufficient antecedent basis for this limitation in the claim. It is not clear if the "test agent" is referring to the recited "compound" in the preceding lines or it is a different entity from the said compound. The method steps of Claim 14 also do not recite "a test agent" as well as "a compound".

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(Note: the instant claim numbers are in bold font.)

11. Claims 14-20, 22, 24 and 28 are rejected under **35 U.S.C. 102(b)** as being anticipated by Clare et al (Conference on Molecular and Functional Diversity of Ion Channels and Receptors, New York NY May 14 – 17, 1998, published as Annals of the New York Academy of Sciences. 1999. 868: 80-83; the published article cited in IDS 10/4/06, citation # C76).

The reference cited was published in April 1999, which is before the earliest possible priority date for the instant application (Provisional filing date of 11/26/1999). The citation for the printed article of the Clare reference from PubMed (see attached PubMed citation print out; downloaded 11/14/06) indicates that this is a "Meeting Paper" and that the meeting was held May 14 –17, 1998, which is more than a year before the earliest possible priority date. The meeting included both oral presentations and poster presentations; the enclosed Table of

Contents for the printed volume clearly lists the reference by Clare et al. as a "poster paper" (see Table of Contents for Volume 868, p. 2; cited in IDS 10/4/06, citation # C75), as opposed to an oral presentation. The reference thus qualifies as a "printed publication" within the meaning of 35 USC 102(b); see MPEP § 2128.01(IV).

The instant claims recite an assay for selecting a compound useful for treating epilepsy or other neurological disorders which modulates inactivation of a sodium channel comprising:

a) an SCN3A nucleic acid sequence which encodes an SCN3A sodium channel or a functional fragment thereof; and

b) assaying a function of said sodium channel; wherein a compound is selected when a difference is observed between the inactivation of said sodium channel in the presence of a test agent, as compared to in the absence thereof.

Clare et al, throughout the publication, teach cloning and functional analysis of the Type III sodium channel from human (p. 80, para 1), which the Type III sodium channel reads on the SCN3A sodium channel (both the nucleic acid sequence and the protein) of **clms 14 and 16**.

The reference teaches assaying the ion channel by using tetrodotoxin (TTX) (p. 80, para 3; p. 81, Figure 1), which the TTX reads on "a compound" of **clms 14 and 16**.

The reference also teaches measuring the inhibition of the sodium channel activity using TTX and compared to controls (p. 81, Figure 1), which reads on step b of **clms 14 and 16**. This also reads on the difference observed between the inactivation (or activity) of the sodium channel

in the presence and absence (e.g. Control and Wash of Figure 1, top panel) of a test agent, as recited in **clms 14 and 16**.

The reference teaches that the Type III sodium channel is from human adult (p. 80, para 2), which reads on the mammalian and human sequence of **clms 15, 17, 18, 19,** and **20**.

The reference also teaches cloning the Type III sodium channel into a vector and expression the channel in host cells (p. 80, para 3), which reads on the recombinant form of **clm 28**.

Although the reference does not explicitly teach the specific nucleic acid sequence (as recited in **clm 22**: SEQ ID No 65) or the protein sequence (as recited in **clm 24**: SEQ ID No 67) of the SCN3A (or Type III) sodium channel, the specific nucleic acid and amino acid sequences are inherent properties of the human Type III (SCN3A) sodium channel. The instant specification discloses that SEQ ID NO 65 shows the cDNA sequence of the human adult form SCN3A (p. 27, line 24 and Sequence Listing of the instant spec.), and SEQ ID No 67 shows the protein sequence of the human adult form of SCN3A (p. 27, line 26 and Sequence Listing of the instant spec.). The instant specification also teaches that the SCN3A is found in the brain (p. 5-6, bridging para), which is the source of the SCN3A nucleic acid of the reference (p. 80, top of para 2). Thus, the SCN3A (in terms of nucleic acid sequence and amino acid sequences) is the same as the ones represented by SEQ ID Nos 65 and 67 of the instant application.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

11/17/06
MY-CHAU T. TRAN
PATENT EXAMINER

SL
Art Unit 1639
11/14/2006